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Theme: 53 Spinal nociceptive mechanisms

TYROSINE KINASE INHIBITOR, GENISTEIN, REDUCES SPINAL NMDA RECEPTOR EXPRESSION INCREASES IN CARRAGEENAN-INDUCED ACUTE ARTHRITIS MODEL

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Protein tyrosine kinases (PTKS) are widely expressed in the central nervous system. One of the major functions for PTKS is regulation of ion channels, such as NMDA receptors. NMDA receptors are a major class of glutamate receptor in the CNS and are involved in injury-evoked persistent pain states. The present study was conducted to determine if the PTK inhibitor, genistein, could reduce NMDA receptor stainability increases that occur after induction of acute arthritis in rats. Joint inflammation was induced by injecting a mixture of 3% kaolin and 3% carrageenan into the knee joint. Genistein (6x10-5 M) or vehicle (50% DMSO in aCSF) was administered spinally with a microdialysis fiber for 1.5h prior to induction of the arthritis. The animals were sacrificed 4h after induction of arthritis, and frozen sections from the lumbar cord of the rats were processing for immunocytochemical localization of NMDAR1. The density of NMDAR1 immunostaining in the dorsal horn of arthritic animals was significantly increased compared to normal rats ($p<0.05$). In the vehicle treated arthritic rats the NMDAR1 stain density was also significantly increased in comparison to the normal rats ($p<0.05$). The results of the present study showed that genistein partially blocked the increased expression of the NMDAR1 in the lumbar spinal cord dorsal horn compared to vehicle treated arthritic rats ($p>0.05$). These results are consistent with our behavioral findings showing that genistein prevents the development of secondary hyperalgesia evoked in response to applied radiant heat. Together these results suggest that tyrosine kinase is involved in NMDA channel activation and modulation of nociceptive and inflammatory responses.
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